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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,572	07/11/2001	Takashi Okuda	010898	4818

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/901,572	OKUDA ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *19 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,5,9-18 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,5,9-18 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4-19-2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 4, 5, 9,-18, and 20 are pending in the present application. In the prior action, mailed on October 20, 2003, claims 1-18, and 20 were under consideration to the extent that they read on DNAs (and compositions thereof) comprising at least one substitution of an Asparaginine in an NXB N-glycosylation site for another amino acid. These claims were rejected. Claim 19 was withdrawn as to a non-elected invention.

2. In the Response of April 19, 2004, the Applicant amended claims 4, 5, 9-18; and canceled claims 1-3, 6-8, and 19.

3. Because this action raises new grounds of rejection, the action is made Non-Final.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on April 19, 2004, is in compliance with the provisions of 37 CFR 1.97. However, the sole reference cited in the IDS was previously made of record, and considered, in the IDS of October 2001. The reference has therefore been crossed out on the April 2004 IDS.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. **(New Rejection)** Claims 4, 5, 10-18, and 20 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The claims read on a DNA molecule or a vector comprising such a molecule, that comprises a portion of a prokaryotic genome that has been modified to remove an NXB site. However, the claims do not require that the sequence encode a protein that performs any particular function. As the Applicant has not provided any utility for a DNA that encodes only a modified NXB site, the claims read on inventions for which no utility has been provided. Further, claim 20 requires that the vector be useful as a vaccine, although the claims do not require that the vector encodes an antigen. Thus, this claim reads on inoperative embodiments. The application indicates that the claimed DNA molecules should encode prokaryotic proteins (page 1, lines 6-12), or antigens for use in DNA vaccines (pages 7-8). It is suggested that the claims be amended such that the DNA molecules include sequences that encode antigens against to induce an immune response against a prokaryotic organism and such that the NXB sites that have been modified are within the sequence encoding the antigens.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. **(Prior Rejection- Maintained)** Claims 1-18, and 20 were rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on

DNA molecules "derived from" prokaryotic cells. It was not clear what the term "derived from" was intended to convey.

The rejection is withdrawn as to claims 1-3, and 6-8, which have been cancelled from the application. The rejection is also withdrawn from claims 4, 10, 11, 13-18, and 20 as the rejected language has been cancelled from these claims.

However, each of claims 5 and 12 still contain the rejected language. While the claims have been amended to state that the DNA sequences comprise a portion of the genome of a prokaryotic cell, it is still unclear what the term "derived from" means. For example, it is unclear if the genome portion "derived from" a prokaryotic cell requires that the genome portion is a part of the genome from which the portion was derived, or if it may include other sequences that have been inserted into the bacterial genome after isolation from other sources. It is suggested that the term "derived" is deleted from the claim such that the claims read on DNA molecules comprising a portion of the genome of a prokaryotic cell, or of a Mycoplasma cell.

9. **(New Rejection- Necessitated by amendment)** Claims 5, and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims have been described above. The claims recites the limitation "wherein said DNA molecule derived from a prokaryotic cell." There is no antecedent basis for this limitation in the claim. It is unclear if the DNA molecule "derived from" the cell is the same as the "portion of the genome of " the prokaryotic cell. Clarification is required.

10. **(Prior Rejection- Withdrawn)** Claims 1-18 and 20 were rejected under 35 U.S.C. 112, second paragraph, as being because it was unclear if the parenthetical statement in the claims was an identification of, or an example of, NXB. In view of the deletion of the parenthesis, and the incorporation of the language into the claim, such that it is clear that the language is describing the NXB site, the rejection is withdrawn.

11. **(Prior Rejection- Withdrawn)** Claims 1-18 and 20 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it was unclear if the N-glycosylation being prevented is the N-glycosylation of the entire protein, or N-glycosylation of the specific NXB site that has been modified. In view of the amendment of the claims, clarifying that the N-glycosylation being prevented is at the NXB site, the rejection is withdrawn.

12. **(New Rejection)** Claims 5 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on DNA molecules wherein "said DNA molecule derived from a prokaryotic cell is a DNA derived from Mycoplasma having the DNA sequence according to SEQ ID NO: 1 or SEQ ID NO: 2." It is unclear if the Applicant is requiring that the claimed DNA molecule is required to comprise SEQ ID NO: 1 or SEQ ID NO: 2."

13. **(New Rejection)** Claims 4, 5, 9-18, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are rejected because it is not clear

in the claims whether the language "a DNA sequence whose sequence comprises a portion of the genome of a prokaryotic cell in which at least one DNA region encoding " an altered NXB site is requiring that the altered NXB site be in the DNA sequence, or if the claims require only that the modification occurs in some region of the genome of which the claimed DNA sequence is a portion. Clarification is required.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. **(New Rejection)** Claims 5 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims have been described above. They read on any DNA from any Mycoplasma having the DNA sequence of SEQ ID NO: 1 or SEQ ID NO: 2. However, the Applicant has not identified any sequences from such Mycoplasma other than the sequences of SEQ ID NO: 1 or SEQ ID NO: 2 themselves.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical

> and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

In the present case, the Applicant has not provided any examples of the claimed DNA molecules other than those that actually comprise SEQ ID NO: 1 or SEQ ID NO: 2. Nor has the Applicant provided any description of DNA sequences from such Mycoplasma such that those in the art would be able to determine which DNA sequences are from cells comprising one of the two sequences from those that do not. In view of the limited written description, while the Applicant has provided sufficient description for DNA molecules that encode Mycoplasma proteins generally, the Applicant has not provided adequate description for the class of DNA molecules that includes any sequence from any Mycoplasma the genome of which comprises SEQ ID NO: 1 or SEQ ID NO: 2.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

17. **(Prior Rejection- Withdrawn)** Claims 1-3, 6, and 7 were rejected under 35 U.S.C. 102(a) as being anticipated by Liu et al., Prot Exp and Pur 19: 304-11 (of record in the June 2003 IDS). In view of the cancellation of these claims, the rejection is withdrawn.

18. **(Prior Rejection- Withdrawn)** Claims 1-3 were rejected under 35 U.S.C. 102(a) as being anticipated by Narhi I (supra). In view of the cancellation of these claims, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. **(Prior Rejection- Maintained)** Claims 1-3, 6, 7, 10, 11, 13, 15-18 and 20 were rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Jacobson et al. (U.S. Patent 5,656,485), or Saitoh et al. (U.S. Patent 5,871,742- of record in the October 2001 IDS) in view of the teachings of Marini et al. (Mol Microbiol 38: 552-64), Essex et al. (U.S. Patent 6,103,238- of record in the June 2003 IDS), and Liu et al. (Prot Exp and Pur, supra), and further in view of the teachings of R. Parekh (Curr Opin Biotech 2: 730-34). Claims 1-3, 6, and 7 have been canceled from the application. The rejection is therefore withdrawn from these claims.

With reference to the Applicant's "note," on page 14 of the Response, that the Jacobson reference teaches the expression of an antigen by bacteria and not by eukaryotic cells, the Applicant's attention is drawn to the end of the same paragraph, on lines 31-33, which state that "expression vectors have also been developed for expression of foreign proteins in eukaryotic cells." Applicant's additional notes regarding the different N-glycosylation processes between prokaryotes and eukaryotes is also noted. These teachings were known in the art, as is demonstrated by the teachings of Parekh, and as was noted in the prior action.

Applicant traverses the rejection on four grounds. First, the Applicant argues that the Jacobson reference does not suggest the claimed invention. Second, the Applicant argues that Essex relates to the expression of a toxic protein, and therefore does not teach the presently claimed invention. Thirdly, the Applicant argues that the art does not teach the use of the viruses disclosed in claims 15-18 (respectively, a pox- or herpes- virus, a virus that infects avians, an avipoxvirus, and a Marek's disease virus). Finally, the Applicant argues that the Liu et al do not teach the use of viral vectors, and therefore does not render the claims obvious.

The Applicant arguments relating to the teachings of each of Jacobson, Essex, and Liu individually are not found persuasive. The rejection is not over the teachings of any one of these references, but on the teachings of the references cumulatively. Both the Court of Customs and Patent Appeals, and the Federal Circuit have indicated that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the present case, because the rejection in not on any one of

the indicated references, but on the indicated combination of references, the traversal is not found persuasive.

The third ground of traversal, that the references do not teach or suggest the use of the indicated viral vectors, is also not found persuasive. On page 6 of the prior action, the rejection refers to column 15, lines 25-36 of the Jacobson reference. This paragraph identifies the indicated viruses as useful vectors. While it is noted that the reference does not specifically relate to the types of Marek's disease virus, it does refer to Marek's disease viruses in general, thereby rendering obvious the use of any particular type of MDV.

The rejection is therefore maintained over claims 10, 11, 13, 15-18, and 20 for the reasons above, and for the reasons of record.

21. **(Prior Rejection- Maintained)** Claims 8 and 14 were rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobson, Saitoh, Liu, Essex, Marini, and Parekh as applied to claims 10, 11, 13, 15-18 and 20 above, and further in view of Nippon Zeon Co., LTD. (EP 0905140-Nippon). Claim 8 has been cancelled from the application. The rejection is therefore withdrawn from this claim.

With respect to claim 14, the Applicant traverses this rejection on the grounds that the Examiner has not presented a general motivation to remove the N-glycosylation sites in prokaryotic proteins for expression in eukaryotic cells for the purpose of making vaccines. This argument is not found persuasive. As was indicated on pages 6-7 of the prior action, the art teaches that the differences in the N-glycosylation between prokaryotic and eukaryotic cells, that such differences may affect the antigenicity of such proteins. The art also teaches that the

problems may be avoided by the modification of the NXB N-glycosylation sites. Thus, the art both provides motivation for the modification of prokaryotic proteins to be expressed in eukaryotic cells generally, and through the teachings relating to the affects on protein antigenicity, the art also suggests the application of these teachings to antigenic proteins, and therefore vaccines. The Applicant's traversal is therefore not found persuasive, and the rejection is maintained over claim 14 for the reasons above, and the reasons of record.

Examiner's Note

22. As was indicated in the prior action, no art rejection is being made over claims directed to the modification of DNA encoding Mycoplasma proteins. This is because the art indicated that the Mycoplasma antigens were effective without such modification, (see, Saito et al. and Yoshida et al., cited in the prior action), thereby providing no suggestion or motivation to specifically modify Mycoplasma proteins for eukaryotic expression. However, the Applicant has demonstrated that such modification is required for Mycoplasma proteins to be effective vaccine antigens. See e.g., App. page 44. While the art indicates that certain benefits may be obtained by preventing N-glycosylation of prokaryotic cell proteins expressed in eukaryotic host cells (e.g. by NXB modification), these teachings are general in nature and do not suggest such modification of genes encoding the Mycoplasma antigens.

Conclusion

23. No claims are allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 7/12/04

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